

**Methods:** Eight *P. aeruginosa* isolates were obtained from clinical samples. PMNs were freshly isolated from healthy human blood. Respiratory burst was assessed by measurement of luminol-enhanced chemiluminescence, and the bactericidal activity of the PMNs was monitored via the loss of bacterial viability (counting of colony-forming units). The bacteria were pre-treated with ciprofloxacin at 0.5, 1.0 and 5.0 times MIC.

**Results:** The pre-treatment had no effect on bactericidal activity: nor on the number of killed bacteria ( $5 \times 10^2 - 2 \times 10^3$ ), neither on the time of action (within 1 h,  $p > 0.1$ ). After pre-treatment the respiratory burst started earlier than in the untreated control (20 versus more than 90 min.). The respiratory burst maximums are in between 1.5–7.0 mV and the response times are 10–30 min.

**Conclusions:** The effects of ciprofloxacin on the bactericidal activity and the respiratory burst differed and exhibited no clear connection with the resistance (MIC) of isolates.

### P:5/10 – Quinupristin/Dalfopristin

#### **WeP136** *In vitro* activity of quinupristin/dalfopristin (synercid) against gram-positive cocci isolated from severe infections in Poland

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**Objectives:** To evaluate susceptibility to quinupristin/dalfopristin (Q-D) of clinical isolates of major Gram-positive pathogens.

**Methods:** Two hundred and eighty-two clinical isolates of various Gram-positive bacteria were used in the study. The collection consisted of strains of *Streptococcus pneumoniae* (n = 40), *S. pyogenes* (n = 10), *Enterococcus faecium* (n = 60), *Staphylococcus aureus* (MRSA, n = 40; MSSA, n = 60) and coagulase-negative staphylococci, CNS (MRCNS, n = 42; MSCNS, n = 30). Susceptibility testing of streptococci was performed with E-tests, and of staphylococci and enterococci – by disc-diffusion method according to NCCLS. Strains observed as resistant to Q-D were additionally characterised by MIC evaluation using E-tests and the agar dilution method in accordance with the NCCLS guidelines.

**Results:** All isolates of *S. pneumoniae*, *S. pyogenes*, and *Staphylococcus spp.* were found susceptible to Q-D. Out of *E. faecium* strains two isolates demonstrated resistance to this antibiotic. These isolates were characterised by MIC values of 4–8 µg/ml. MICs of Q-D for *S. pneumoniae* strains were evaluated as 0.5–1.0 µg/ml, and for *S. pyogenes* strains – as 0.25–0.38 µg/ml.

**Conclusions:** The study revealed a very high *in vitro* activity of quinupristin/dalfopristin against major Gram-positive pathogens. The antibiotic may be very useful in treatment of serious infections caused by multiresistant strains (e.g. MRSA and vancomycin-resistant *E. faecium*).

#### **WeP137** *In vitro* activities of quinupristin-dalfopristin, linezolid, and new quinolones against over 1200 clinical isolates of gram-positive bacteria in Taiwan

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**Objectives:** To determine the *in vitro* activities of quinupristin-dalfopristin, linezolid, and new quinolones for recent clinical isolates of gram-positive bacteria.

**Methods:** A total of 1210 nonduplicate, clinical isolates of gram-positive bacteria were recovered patients mainly treated at National Taiwan University Hospital (NTUH) from January 1996 to December 1999. These isolates included 100 blood isolates of methicillin-resistant *Staphylococcus aureus*, 461 of coagulase-negative staphylococci, 267 of *S. pneumoniae*, 120 of viridans streptococci, 150 of VRE (vancomycin MICs of  $\geq 32$  µg/ml), 35 of *Leuconostoc spp.*, 8 of *Pediococcus spp.*, and 69 of *Lactobacillus spp.* MICs of these isolates for 12 antimicrobial agents were determined by using the standard methods recommended by the National Committee for Clinical Laboratory Standards (NCCLS).

**Results:** Linezolid demonstrated the most potent activity (MIC<sub>90</sub>s, 2 µg/ml) against all isolates tested, including MRSA, VRE, and vancomycin-resistant bacteria. Quinupristin-dalfopristin showed limited activity against vancomycin-resistant *E. faecium* (MIC<sub>90</sub>, 16 µg/ml), *Pediococcus* (MIC<sub>90</sub>, 128 µg/ml), *Leuconostoc* (MIC<sub>90</sub>, 128 µg/ml), and *Lactobacillus spp.*

(MIC<sub>90</sub>, 16 µg/ml). Moxifloxacin and trovafloxacin had good activity against these isolates except for ciprofloxacin-resistant VRE and methicillin-resistant staphylococci.

**Conclusions:** Linezolid appears to be a promising antimicrobial agent for the treatment of infections caused by gram-positive bacteria. Quinupristin-dalfopristin is not a suitable alternative for managing infections due to vancomycin-resistant *E. faecium* in Taiwan.

#### **WeP137B** Antimicrobial combinations against MRSA

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**Objective:** To study the antibacterial effect of combinations of teicoplanin (T) and quinupristin/dalfopristin (Q/D) with broad-spectrum antimicrobial agents against MRSA (methicillin-resistant *Staphylococcus aureus*).

**Methods:** 10 diverse clinical isolates of MRSA were studied. MICs were determined by Etest. Time-kill studies were performed using a broth macrodilution method. Combinations of T and Q/D were studied with ceftazidime, cefepime, piperacillin-tazobactam and meropenem.

**Results:** T and Q/D alone had cidal and static activity respectively against the isolates tested. Antagonism was demonstrated between T and Q/D for 9/10 isolates. Synergic or antagonistic effects were not generally seen with combinations of either T or Q/D and broad-spectrum antimicrobial agents.

**Conclusions:** This study did not suggest any potential benefit or contra-indication to the concurrent use of selected broad-spectrum antimicrobials during treatment of MRSA infection with either T or Q/D. A potential for antagonism between T and Q/D was demonstrated.

### P:5/11 – Rifampicin

#### **WeP138** Relationship between *rpoB* mutations in *Staphylococcus aureus* and antimicrobial activities of rifampicin and KRM-1648

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**Objectives:** This study was aimed at determining the *in vitro* antibacterial activities of the rifamycin derivatives rifampicin and KRM-1648 against *Staphylococcus aureus* and at correlating the level of resistance to both rifamycins with the genetic alterations in the *rpoB* gene.

**Methods:** The *in vitro* antibacterial activities were determined against 150 *Staphylococcus aureus* isolates, including 50 rifampicin-sensitive (Rif<sup>s</sup>) methicillin-sensitive *Staphylococcus aureus* (MSSA), 50 Rif<sup>r</sup> methicillin-resistant *Staphylococcus aureus* (MRSA), and 50 rifampicin-resistant (Rif<sup>r</sup>) MRSA. Concerning Rif<sup>r</sup> MRSA, the genetic alterations in the *rpoB* gene were determined by PCR amplification and sequencing.

**Results:** The MICs of rifampicin and KRM-1648 for 90% of Rif<sup>r</sup> *Staphylococcus aureus* isolates tested were 0.016 and 0.001 µg/ml, respectively. Missense mutations within a 204 bp fragment covering clusters I and II of the rifampicin resistance region could be demonstrated in all Rif<sup>r</sup> MRSA isolates. The *in vitro* susceptibility testing of rifampicin and KRM-1648 against Rif<sup>r</sup> MRSA isolates revealed different activities of the rifamycins with respect to specific mutations within *rpoB*. Specific mutation sites could be identified which exhibited high-level cross-resistance to both rifamycins, while a subset of mutations were associated with an up to 100 fold better activity of KRM-1648.

**Conclusions:** The results provide evidence that the new rifamycin KRM-1648 is a potent antimicrobial that displays a high activity even against a subset of rifampicin-resistant *Staphylococcus aureus* isolates.

#### **WeP139** Rapid detection of rifampicin resistance in *Mycobacterium tuberculosis* clinical isolates using mycobacteriophages

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**Objectives:** To standardise a rapid, non-laborious and low-cost assay to study the susceptibility of *M. tuberculosis* (MTB) clinical isolates to rifampicin by using mycobacteriophage D29.